

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 65248

**Title:** Current guidelines for the management of celiac disease: A systematic review with comparative analysis

**Provenance and peer review:** Invited manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 03307766

**Position:** Editorial Board

**Academic degree:** MD, MSc, PhD

**Professional title:** Associate Professor, Director, Doctor

**Reviewer's Country/Territory:** Kazakhstan

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-03-02

**Reviewer chosen by:** Man Liu

**Reviewer accepted review:** 2021-05-21 02:02

**Reviewer performed review:** 2021-05-22 14:27

**Review time:** 1 Day and 12 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="checkbox"/> ] Anonymous [ <input type="checkbox"/> ] Onymous Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No
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## SPECIFIC COMMENTS TO AUTHORS

INTRODUCTION - "Celiac disease (CD) is an immune-mediated REACTION to gluten characterized....". CD is a well-defined immune-mediated DISEASE, not just a "reaction". - "CD's epidemiology...". I wouldn't use the genitive. - What the authors mean with the expression "in the age of gluten-related disorders": this is not clear. - "CD remains a largely underdiagnosed disease [3]. Simultaneously, misdiagnosis of CD is becoming an emergent problem in in the age of gluten-related disorders [4-6]. The authors correctly suggest that the correct and timely diagnosis of CD is still a problem; however, the cited references (n.3: 2007; n.4: 2016; n.5: 2009; n.6: 2009) are not recent and I do not think they can support this concept as an ongoing issue. Therefore, I suggest the authors to change all these references with more recent and appropriate ones. Moreover, by doing that, the authors should emphasize the concept that such a problem is present everywhere but could especially affect developing countries and may have a higher impact in children (see some very recent papers where this issue is clearly discussed across different geographical/economical setting: World J Gastroenterol. May 21, 2021; 27(19): 2251-2256, doi: 10.3748/wjg.v27.i19.2251; Eur J Pediatr. 2021 Jun;180(6):1941-1946. doi: 10.1007/s00431-021-03974-8; PLoS One. 2020 Jan 2;15(1):e0226546. doi: 10.1371/journal.pone.0226546; J Pediatr Gastroenterol Nutr. 2019 Oct;69(4):443-448. doi: 10.1097/MPG.0000000000002424; Dig Liver Dis. 2021 Apr;53(4):504-505. doi: 10.1016/j.dld.2021.01.008). These articles may also provide insightful suggestions for the discussion and perspective section. - "...avoid life-threatening complications deriving from unrecognised CD...". I think the authors should define/explain what these complications are or may be. Of course, this sentence should be supported by additional

and appropriate references. In general, this paragraph should be supported by references, that are not present at all. **LITERATURE SEARCH** - The authors define this manuscript as “systematic review”. The authors should provide a figure including the PRISMA flow diagram, in addition to describe in detail all the phases in the text. The literature search is the first phase and, therefore, it should be a part of a more comprehensive Materials and Methods section, including the specific aims, protocol, search strategy and data extraction. In part, this information is already present, but needs to be completed and included in a well-structured materials and methods section. - Probably, the authors should also introduce and explain here their analysis strategy, according to the structure that they gave to the results section, in my opinion. **RESULTS (/DISCUSSION)** - Indeed, I think it’s interesting this structure with clear questions/points, I mean analyzing specific diagnostic aspects across the different guidelines retrieved through their search strategy. And I find very nice the tables that they drafted to schematically summarize their results. - However, I do not agree with the fact that the authors merged results and discussion, because each subsection of the results includes both aspects, actually. The authors should completely revise this organization and separate the results from the discussion. In the results, they should present their interesting and “objective” findings summarized in the tables and, therefore, these tables should drive the manuscript at this level. - For instance, in section 1: the results are the description and comparison of the guidelines recommendations according to different symptoms (gastrointestinal vs. extra-gastrointestinal, inclusion of specific symptoms, etc.). Then, the authors can arrange a different section (discussion) with the same substructure by discussing and commenting the different points. This manuscript organization would be much more appropriate for a systematic review, which aims to be objective and not narrative. **CONCLUSION** - the conclusion should not include any references (or very few). Here,



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the authors should provide and summarize their take-home and practical messages very clearly. REFERENCES - to be critically revised and, then, completed and updated. Indeed, out of around 70 references used after the search strategy, only 15-16 were published after 2015; I think the authors may have found more recent and original references for many aspects (e.g. HLA testing, refractory CD).

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**Peer-review model:** Single blind

**Reviewer's code:** 03538272

**Position:** Peer Reviewer

**Academic degree:** BM BCh

**Professional title:** Doctor, Research Fellow, Staff Physician

**Reviewer's Country/Territory:** Australia

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-03-02

**Reviewer chosen by:** Man Liu

**Reviewer accepted review:** 2021-05-26 03:11

**Reviewer performed review:** 2021-05-26 03:47

**Review time:** 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



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<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="radio"/> ] Anonymous [ <input type="radio"/> ] Onymous Conflicts-of-Interest: [ <input type="radio"/> ] Yes [ <input checked="" type="radio"/> ] No
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## **SPECIFIC COMMENTS TO AUTHORS**

The authors have performed a comparison of current guidelines for celiac disease focusing on seven major guidelines. They compare and contrast suggestions across the guidelines and provide a useful appraisal for practising clinicians. The manuscript has a good format and provides important information. The only further suggestion to assist clinicians would be the possibility of adding additional information in a Table or Figure to help clinicians with the overall clinical implications of the recommendations. A Table summarizing individuals or symptoms that should be considered as indications for testing for celiac disease will benefit the initial section. A figure going through a suggested diagnostic algorithm for patients with suspected celiac disease and when the major tests would be used would be valuable for clinicians. Minor points: Table 9: there needs to be a space between “GFD” and “which”

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**Peer-review model:** Single blind

**Reviewer's code:** 05458182

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Deputy Director

**Reviewer's Country/Territory:** Russia

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-03-02

**Reviewer chosen by:** Man Liu

**Reviewer accepted review:** 2021-05-21 03:30

**Reviewer performed review:** 2021-05-26 18:00

**Review time:** 5 Days and 14 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="checkbox"/> ] Anonymous [ <input type="checkbox"/> ] Onymous Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No
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## SPECIFIC COMMENTS TO AUTHORS

The title reflects the main subject of the manuscript. The abstract summarizes and reflects the work described in the manuscript. The key words reflect the focus of the manuscript. The tables have a good quality and appropriately illustrative of the paper contents. The manuscript meets the requirements of use of SI units. The manuscript cites appropriately the latest, important and authoritative references. The manuscript is well organized and presented. The style, language and grammar are accurate and appropriate. The manuscript met the requirements of ethics. The manuscript is a systematic review and comparison of the most relevant international recommendations and national guidelines for the diagnosis and treatment of celiac disease. The search was carried out in the Pubmed database for the period from 2010 to 2021. As a result of the analysis, significant similarities on key issues of diagnosis and treatment of patients with celiac disease were found. At the same time, the revealed differences in international recommendations identified the most controversial issues and opened up prospects for their further study. Most interesting is the discussion by the authors of the possibility of diagnosing celiac disease without biopsy. These guidelines are available for the diagnosis of celiac disease in children. The main controversial point is the possibility of diagnosing celiac disease without biopsy in adults. Significant differences were found in the follow-up of celiac disease patients. The recommendations reflected in the national guidelines are based on different medical surveillance systems. In this case, it is very important which specialist (dietician, gastroenterologist, primary care physician, etc.) will be responsible for further monitoring of the celiac disease patient. Most guidelines show no preference for a specific specialist although for adult patients with celiac



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disease it is essential to conduct further observation with an assessment of blood values, histological structure of the small intestine and number of other criteria enabling to monitor the development of adverse complications (autoimmune, oncological). Another important point is the follow-up strategy for celiac disease patients. There are significant differences in the set of examination methods, the frequency of procedures and the age at which the examination should be carried out. All of the above points and some others were revealed thanks to the analysis carried out and discussed in detail by the authors in the presented review. The manuscript is of great scientific value, as it has identified the direction to follow for further study of the celiac disease.

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**Peer-review model:** Single blind

**Reviewer's code:** 03544596

**Position:** Editorial Board

**Academic degree:** MD

**Professional title:** Associate Professor

**Reviewer's Country/Territory:** Turkey

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-03-02

**Reviewer chosen by:** Man Liu

**Reviewer accepted review:** 2021-05-26 07:16

**Reviewer performed review:** 2021-05-27 07:10

**Review time:** 23 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



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<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="checkbox"/> ] Anonymous [ <input type="checkbox"/> ] Onymous Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No
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#### **SPECIFIC COMMENTS TO AUTHORS**

Thanks to the authors for the systematic review of celiac disease. Tables are complex, tables should be simple and understandable. There are minor language errors.

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Peer-review model:** Single blind

**Reviewer's code:** 03307766

**Position:** Editorial Board

**Academic degree:** MD, MSc, PhD

**Professional title:** Associate Professor, Director, Doctor

**Reviewer's Country/Territory:** Kazakhstan

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-03-02

**Reviewer chosen by:** Li-Li Wang

**Reviewer accepted review:** 2021-11-16 05:21

**Reviewer performed review:** 2021-11-16 08:52

**Review time:** 3 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Peer-reviewer</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [ ] Yes [Y] No

#### **SPECIFIC COMMENTS TO AUTHORS**

The authors addressed appropriately or clearly answered all the comments, overall. I have no additional and relevant comments. In detail, as regards point 8, even if the authors kept their original organization, they explained their point and I can accept their decision.